

C1  
cont  
sequence of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, or degenerate variants thereof, and wherein said nucleic acid encodes the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, or SEQ ID NO: 48, respectively.

---

36. (Amended) A substantially pure nucleic acid having a polynucleotide sequence that has at least 50% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

C2  
37. (Amended) The nucleic acid of claim 36, having a polynucleotide sequence that has at least 85% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

38. (Amended) The nucleic acid of claim 37, having a polynucleotide sequence that has at least 95% sequence identity to SEQ ID NO: 1 over the entire length of SEQ ID NO: 1.

---

C3  
41. (Amended) A substantially pure nucleic acid having a polynucleotide sequence that has at least 50% sequence identity to the corresponding region of SEQ ID NO: 1, wherein said nucleic acid comprises a naturally-occurring mammalian methionine synthase reductase mutation or polymorphism.

42. (Amended) The nucleic acid of claim 41, having a polynucleotide sequence that has at least 85% sequence identity to the corresponding region of SEQ ID NO: 1.

43. (Amended) The nucleic acid of claim 42, having a polynucleotide sequence that has at least 95% sequence identity to the corresponding region of SEQ ID NO: 1.

---

Add the following new claims 48-53.

48. (New) The nucleic acid of claim 47, wherein said binding site comprises a sequence that is at least 70% identical to one of the following sequences:

- C4
- (a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),
  - (b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),
  - (c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),
  - (d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),
  - (e) FVFNIVEFLSTATT (SEQ ID NO: 56),
  - (f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),
  - (g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),
  - (h) SFSRDA (SEQ ID NO: 59),
  - (i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV  
(SEQ ID NO: 60), or
  - (j) KRYLQDIWS (SEQ ID NO: 61).

49. (New) The nucleic acid of claim 48, wherein said binding site comprises a sequence that is identical to one of the following sequences:

- (a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),
- (b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),
- (c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),
- (d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),
- (e) FVFNIVEFLSTATT (SEQ ID NO: 56),
- (f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),
- (g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),
- (h) SFSRDA (SEQ ID NO: 59),
- (i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV  
(SEQ ID NO: 60), or

(j) KRYLQDIWS (SEQ ID NO: 61).

50. (New) The nucleic acid of claim 47, wherein said binding site comprises any one of SEQ ID NOs: 25-40.

51. (New) The nucleic acid of claim 4 or 41, wherein the administration of said nucleic acid to a subject leads to a decrease in the activity of a mutant or polymorphic methionine synthase reductase polypeptide in said subject.

52. (New) The nucleic acid of claim 51, wherein the administration of said nucleic acid leads to a decrease in the activity of said mutant methionine synthase reductase polypeptide.

53. (New) The nucleic acid of claim 4 or 41, wherein said nucleic acid comprises said naturally-occurring mammalian methionine synthase reductase mutation.

---

In the Specification

Kindly replace the Sequence Listing with the enclosed amended Sequence Listing.

REMARKS

The invention features the cloning of mammalian methionine synthase reductase. Accordingly, the invention provides wild-type and mutant mammalian methionine synthase reductase nucleic acids.

Examination of claims 1-5 and 35-47 is reported in the present Office Action. Claims 36-38 and 41-43 were objected to because of improper sequence identifiers. Claims 3 and 47 were rejected under 35 U.S.C. § 112, second paragraph, and claims 1, 2, 4, 5, and 35-47 were rejected under 35 U.S.C. § 112, first paragraph. Each of the rejections is addressed below in the order that they appear in the Office Action.